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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/664,610	09/16/2003	Charles Wilson	23239-538 (ARC-38)	5499

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EXAMINER

HUMPHREY, LOUISE WANG ZHIYING

ART UNIT	PAPER NUMBER
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1648

MAIL DATE	DELIVERY MODE
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05/30/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/664,610

Applicant(s)

WILSON ET AL.

Examiner

Louise Humphrey, Ph.D.

Art Unit

1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 February 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 42-70 is/are pending in the application.
- 4a) Of the above claim(s) 42-45, 58, 59 and 65 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 46-57, 60-64 and 66-70 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>10/19/06</u> | 6) <input type="checkbox"/> Other: _____ |

Response to Arguments

This Office Action is in response to the amendment filed 26 February 2007.

Claims 42-70 are pending. Claims 42-45, 58, 59, and 65 are withdrawn. Claims 46-57, 60-64, and 66-70 are under final rejection.

Claim Rejections - 35 U.S.C. §112

The following is a quotation of the second paragraph of 35 U.S.C. §112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claims 46-57, 60-64, and 66-70 under 35 U.S.C. §112, second paragraph, as being indefinite is maintained. The term "target partner" is confusing. That is, it is unclear if the "target partner" is a receptor, a coenzyme, a cofactor, a substrate, an enzyme, a recruitment protein or a binding partner for the target in an enzyme complex.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The rejection of claims 46-57, 60-64, and 66-70 under 35 U.S.C. §103(a) as being obvious over Griffin *et al.* (US 5,756,291) is maintained.

The instant invention is a method of identifying an aptamer that binds to a target, the target being capable of binding a target partner, wherein the binding of the aptamer to the target increases the binding affinity of the target for the target partner.

Examiner's rejection in the Action mailed on 25 September 2006 is as follows:

Griffin *et al.* describe a method for identifying aptamers that specifically bind target molecules such as cell surface molecules or glycoproteins (Abstract and col. 13, lines 40-47). Griffin *et al.* describe various methods (col. 42-80) to identify specific binding oligonucleotide sequences by incubating a pool of oligonucleotides with support-bound target molecules and detaching the resulting target-oligonucleotide complexes from the support. See col. 1, lines 32-59. Specifically, Griffin *et al.* describe a preferred variation, for selection of aptamers that bind to surface antigens, involving a procedure wherein negative selection is first carried out followed by a positive selection. In accordance with this procedure, a pool of random oligonucleotides is combined with a tissue culture medium. The oligonucleotides are allowed to remain in contact with cell cultures for a sufficient period of time to allow binding between oligonucleotides and cell surfaces which lack the target molecule. When this binding occurs, a negative selection process has been carried out, i.e., oligonucleotides which are not the desired aptamers can be eliminated by their binding to nontarget surfaces. Following this negative selection, a positive selection step is carried out. This is done by combining the oligonucleotides which did not bind to the surfaces lacking target molecules thereon with a cell culture containing the target molecule on their surface. Such a negative-positive selection protocol can be carried out in a medium containing human or bovine serum in order to select aptamers under simulated physiological conditions. See the paragraph bridging columns 29-30. The resulting complexes are removed from the uncomplexed oligonucleotides and the bound aptamer population is recovered and amplified as usual. See col. 29, lines 17-27. Most relevantly, Griffin *et al.* disclose exemplary approaches involving the use of multiple selections to derive aptamers with highly specific properties, as an example, a round of selection involves selecting those oligonucleotides that bind to a complex between a target, thrombin, and a target partner, thrombomodulin. See col. 24, lines 1-13. A diverse pool of oligonucleotides can be in the first generation, which can subsequently be used to generate a second generation that is more target-based. See the paragraph bridging col. 35-36.

Although Griffin *et al.* do not disclose the specific application as claimed, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the negative-positive aptamer selection protocol of Griffin *et al.* by designating the bound target-target partner/analog complex as the "target molecule" and the unbound target or target partner/analog by itself as the "nontarget molecule" for the purpose of the selecting aptamers that facilitate the complex formation. The skilled artisan would have been motivated to do so to develop aptamers that function as a carrier that delivers the therapeutic cargo to the specific desired binding site. There

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would have been a reasonable expectation of success, given the general protocol of aptamer negative-positive selection protocol with suggested variations to obtain desired aptamers and the teaching that a wide variety of materials, including cell surface glycoproteins, can serve as targets, as taught by Griffin *et al.* Thus, the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Applicants argue that the exemplary approach indicated in Griffin is not for the purpose of selecting aptamers that facilitate complex formation rather it is for selecting aptamers that block thrombin activity towards fibrinogen while not interfering with thrombin binding to thrombomodulin and its activity towards Protein C. The examiner has already stated in the previous Office Action, see above, that the Griffin patent does not expressly disclose the selection of aptamers that facilitate complex formation. However, the suggestion to modify the Griffin method to select for complex-stabilizing aptamers is well within the knowledge generally available to one skilled in the art. The selection conditions and stringency are to be tailored for each application. In the instant case, the target for the aptamers is a complex of two domains, a "target" and its partner. The word "target" is not limited to a single molecule, but to whatever moiety the aptamers are selected to bind to, as evidenced by Griffin's suggestion that the invention, in another aspect, is directed to *complexes* of the target molecules and the aptamers and to methods to obtain and to use the aptamers. See column 11, lines 34-37. It would be obvious to add complex-forming target molecules during the selection of aptamers to identify aptamers that bind to the complex. The only modification of the Griffin selection method is to add one more type of molecules that form a complex with the first type of molecules. Therefore, the instant invention is obvious over Griffin *et al.*

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Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

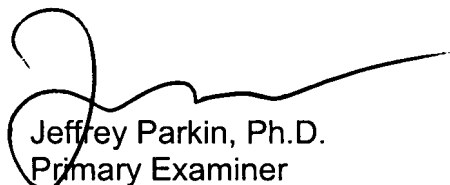
A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Correspondence

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey, Ph.D. whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9:30 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can be reached at 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



Jeffrey Parkin, Ph.D.
Primary Examiner
23 May 2007



Louise Humphrey, Ph.D.
Assistant Examiner